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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,153	09/04/2002	Robert E Nordon	4137-9	2271

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NIXON & VANDERHYE, PC  
901 NORTH GLEBE ROAD, 11TH FLOOR  
ARLINGTON, VA 22203

EXAMINER
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BEISNER, WILLIAM H

ART UNIT	PAPER NUMBER
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1744

DATE MAILED: 07/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No. 10/089,153	Applicant(s) NORDON, ROBERT E	
	Examiner William H. Beisner	Art Unit 1744	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 10 May 2005.  
 2a) ☐ This action is FINAL.                      2b) ☒ This action is non-final.  
 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-70 is/are pending in the application.  
     4a) Of the above claim(s) 1-44 is/are withdrawn from consideration.  
 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.  
 6) ☒ Claim(s) 45-70 is/are rejected.  
 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.  
 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.  
 10) ☒ The drawing(s) filed on 04 September 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
     a) ☐ All    b) ☐ Some \* c) ☐ None of:  
         1. ☐ Certified copies of the priority documents have been received.  
         2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
         3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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## **DETAILED ACTION**

### ***Election/Restrictions***

1. Applicant's election of Group III, Claims 45-70, in the reply filed on 5/10/2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 1-44 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 5/10/2005.

### ***Information Disclosure Statement***

3. Note while the prior art of WO 91/10425 and WO 05/27041 has been made of record, the non-patent references of Lloyd et al. and Gerlach et al. that were cited in the International Search Report have not been made of record because they have not been provided by the applicants and are not readily available to the examiner.

### ***Priority***

4. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

### ***Claim Rejections - 35 USC § 112***

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5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 45-70 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 45, "the cell biomass" lacks antecedent basis. Note while the claim recites that the device is intended to be used with cells, the claim is silent and/or fails to distinguish with respect to a "cell biomass". Also the claim limitation that the "circulation means being response to the cell biomass" is also indefinite. The metes and bounds of the claims are not readily apparent from this claim language. Claims 46-70 are indefinite based on their dependencies on indefinite claim 45.

In claim 51, it is not clear if an inner diameter or an outer diameter is being claimed.

In claim 53, "the cellular biomass" lacks antecedent basis. Note claim 45 previously employs the language "cell biomass".

***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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8. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. Claims 45-53, 55-58 and 60-70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Slowiaczek et al.(US 5,763,194) in view of Amiot et al.(US 5,202,254).

The reference of Slowiaczek et al. discloses a bioreactor for the proliferation of and growth of cells that includes the use of hollow fiber membranes for the containment of cells therein and formed of a semipermeable material that is permeable to at least nutrient, regulator or metabolite and positioned within a housing to define an acellular space (See Figures 4 and 5 and column 11, lines 16-58). The housing has inlet and outlet structures communicating with the acellular space to define an acellular flow path (See Figures 4 and 5). The device includes a liquid flow circuit providing fluid communication with the inlet and outlet (See column 11, lines 23-26).

Claim 45 first differs by reciting that the semipermeable material is permeable to at least nutrient, regulator or metabolite but is not permeable to at least protein required for proliferation, differentiation and/or genetic modification.

The reference of Amiot et al. discloses that it is known in the art to culture cells on one side of a semipermeable membrane wherein media containing oxygen, nutrients and other chemical stimuli is transported through the semipermeable membrane from a media side to the

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cell side and while waste products and contaminating proteins are transported from the cell side to the media side of the membrane (See column 1, lines 16-46). The reference also discloses that the molecular weight cut-off of the membrane is chosen so as to provide the transfer discussed previously while maintaining cellular product and serum on the cell side of the membrane (See column 1, lines 34-39, and column 6, lines 49-56).

In view of this teaching, it would have been obvious to one of ordinary skill in the art to modify the molecular weight cut-off of the membrane of the primary reference for the known and expected result of providing a membrane that maintains cellular product and/or growth factor (serum) on the cell side of the membrane while still providing for the exchange of cell nutrients and waste products as is contemplated by the reference of Amiot et al.

Claim 45 further differs by reciting that the circulation system that circulates media through the acellular space is responsive to the cell biomass.

The reference of Amiot et al. discloses that it is known in the art to determine the glucose utilization and lactate production rates in a hollow fiber bioreactor device and adjust the medium feed rate in response to these measured rates (See column 7, lines 7-19).

In view of this disclosure, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the system of the modified primary reference so that the circulation system for the acellular space is responsive to the cell biomass for the known and expected result of maintaining predetermined metabolite levels. Note whether the response is provided manually or by automated means is not sufficient to patentably distinguish over the prior art references because providing an automatic or mechanical means to replace a manual activity which accomplished the same result is not sufficient to distinguish over the prior art.

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In re Venner, 262 F.2d 91, 95, 120 USPQ 193, 194 (CCPA 1958).

With respect to claim 46, the combination of the references as discussed above would result in a device wherein the lumens of the hollow fibers contain cells and at least one protein required for proliferation, differentiation and/or genetic modification of the cells.

With respect to claim 47, the combination of the references as discussed above would result in a device wherein the acellular space would contain media including at least one substance required for the proliferation of the cells.

With respect to claim 48, the substance can be oxygen, glucose or amino acids (See column 11, lines 28-29, of Slowiaczek et al.).

With respect to claims 49 and 50, the hollow fiber membrane can be cellulose (See column 2, lines 28-34, of Slowiaczek et al.).

With respect to claim 51, in the absence of a showing of criticality and/or unexpected results, it would have been obvious to one of ordinary skill in the art to determine the optimum dimensions of the hollow fiber membrane while providing the required molecular weight cut-off and maintaining the structural integrity of the fibers.

With respect to claim 52, the reference of Amiot et al. discloses that the use of pumps for circulating media relative to the acellular side of the membrane in a culture device is conventional in the art. As a result, it would have been obvious to one of ordinary skill in the art to employ a pump in the system of the modified primary reference for the known and expected result of providing an art recognized means for circulating the culture media within a membrane bioreactor system.

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With respect to claim 53, the cellular biomass is determined using lactate output (See column 7, lines 7-19, of Amiot et al.).

With respect to claims 55-58, the reference of Amiot et al. discloses the use of a gas exchange cartridge (38, 56) for controlling the oxygen and carbon dioxide content of the acellular media. The use of silicone membranes in oxygenation devices is notoriously well known in the art and would have been obvious for the known and expected result of providing an art recognized structure for oxygenating the culture media.

With respect to claim 60, the acellular media is recycled (See Figures 1, 2 and 3 of Amiot et al.).

With respect to claim 61, the reference of Amiot et al. discloses that the use of a pump and inlet (66) is known in the art for adding fresh media. As a result, it would have been obvious to provide the system of the modified primary reference with a means for adding fresh medium for the known and expected result of replacing spent media over the length of the culture process.

With respect to claims 62-65, the lumens of the hollow fibers include ligands (See column 2, lines 41-45; Figure 5; and column 11, lines 16-59, of Slowiaczek et al.).

With respect to claims 66-68, the cells are haematopoietic cells (See column 11, lines 46-59, of Slowiaczek et al.).

With respect to claim 69, the device is capable of both cell separation and culture.

With respect to claim 70, in the absence of further positively recited structure, the device is considered to be portable.



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10. Claim 54 is rejected under 35 U.S.C. 103(a) as being unpatentable over Slowiaczek et al.(US 5,763,194) in view of Amiot et al.(US 5,202,254) taken further in view of Folena-Wasserman et al.(US 5,252,216).

The combination of the references of Slowiaczek et al. and Amiot et al. has been discussed above.

Claim 54 differs by reciting that oxygen uptake is used as an indicator for cellular biomass.

The reference of Folena-Wasserman et al. discloses that oxygen uptake is also an indicator of cellular biomass in a culture device (See column 12, lines 5-32).

In view of this teaching, it would have been obvious to one of ordinary skill in the art to employ oxygen uptake as an additional parameter for controlling the flow of media within the culture device as suggested by the reference of Folena-Wasserman et al.

11. Claim 59 is rejected under 35 U.S.C. 103(a) as being unpatentable over Slowiaczek et al.(US 5,763,194) in view of Amiot et al.(US 5,202,254) taken further in view of Gebhard et al.(US 5,126,238).

The combination of the references of Slowiaczek et al. and Amiot et al. has been discussed above.

Claim 59 differs by reciting that the device includes a device for controlling the temperature of the culture media.

The reference of Gebhard et al. discloses that it is conventional in the art to employ a loop heater for controlling the temperature of the culture media (See column 8, lines 19-27).

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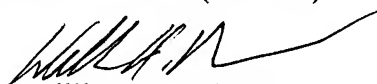
In view of this teaching, it would have been obvious to one of ordinary skill in the art to provide the system of the modified primary reference with a heater device for controlling the temperature of the culture media for the known and expected result of maintaining the viability of the cells by maintaining proper culture conditions including temperature.

### *Conclusion*

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to William H. Beisner whose telephone number is 571-272-1269. The examiner can normally be reached on Tues. to Fri. and alt. Mon. from 6:15am to 3:45pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John Kim can be reached on 571-272-1142. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



William H. Beisner  
Primary Examiner  
Art Unit 1744

WHB